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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,156	03/09/2005	Masahiko Sisido	SAE-0031	1834

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RADER FISHMAN & GRAUER PLLC
LION BUILDING
1233 20TH STREET N.W., SUITE 501
WASHINGTON, DC 20036

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/527,156	SISIDO ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *2-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-9-05,6-3-05,6-2-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Sequence Rule Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

CFR §1.821(d) reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims or the patent application.

Figures 4-5 and 7 of the instant application contain nucleic acid sequences which are not preceded by "SEQ ID NO:". Applicants are reminded that either the brief description of drawings for the Figures or Figures themselves should make a reference to the sequences by use of the sequence identifiers in accordance with CFR §1.821 through 1.825. Applicants are also reminded that the nucleic acid sequences depicted in Figures 4-5 and 7 must be entered in the paper copy of sequence listing as well as CRF. See Notice to Comply. Any response to this action must correct this deficiency, as this requirement will not be held in abeyance.

Response to Arguments/Election/Restriction

Applicant's election with traverse of claims 12-15 and 17-21 in the reply filed on September 29, 2006 is acknowledged. The traversal is on the ground(s) that there is no serious burden on the examiner to search the two distinctly grouped inventions. This is not found persuasive because the instant application is filed under 35 U.S.C. 371 and 37 CFR 1.495, which therefore is subject to the "unity of invention" rule. See MPEP Chapter 1800 regarding 37 CFR §1.475, for example. Further, the issue of "search burden" is neither stated nor asserted in the Office action mailed to the applicant on September 1, 2006. Since the instant application is not a U.S. filed application, the rules stated in MPEP 803 regarding search burden does not apply, thus applicant's argument is irrelevant and moot.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 1, 16, and 22-25 have been cancelled by applicants. Hence, claims 2-15 and 17-21 are pending and claims 12-15 and 17-21 are currently under examination on the merits.

Priority

Receipt is acknowledged of the certified copy of the Japanese application No. 2002-262301 submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted, however, that the document is in non-English language and thus the examiner cannot verify whether the foreign document adequately describes and supports the instantly claimed invention. Further, an English translation of said document has not been made of record

in accordance with 37 CFR 1.55. See MPEP § 201.15.

Accordingly, the priority benefit to the Japanese document is denied and the effective filing date for the instant application will be the filing date of the PCT/JP03/11391, September 5, 2003.

Information Disclosure Statement

The information disclosure statement filed on March 9, 2005 has been placed in the application file, but the information referred to as Citation Nos. CB, CE, CF, and CG has been considered as to the merits as far as the figures and titles because the text of the above-mentioned citations is written in a non-English language.

Specification

The disclosure is objected to for containing sequence rule non-compliant subject matter in Figures 4-5 and 7. See Notice to Comply. Appropriate correction is required.

Claim Objections

Claim 17 is objected to because of the following informalities: Line 6 recites "consisted of", which should instead read "consists of". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "close to" in claim 12, line 5 is a relative term which renders the claim indefinite. The term "close to" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. That is, one skilled in the art cannot recognize the metes and bounds set forth by the term "close to" because it is unclear what constitutes the claimed parameters of distance proximity embraced by the term "close to", thus rendering claim 12 and its dependent claims indefinite.

The term "in advance" in claim 13, line 3 is a relative term which renders the claim indefinite. The term "in advance" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. That is, one skilled in the art cannot recognize the metes and bounds set forth by the term "in advance" because it is unclear what range of time constitutes the term "in advance", thus rendering claim 13 and its dependent claims indefinite.

The term "high catalytic activity" in claim 18, line 3 is a relative term which renders the claim indefinite. The term "high catalytic activity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. That is, one skilled in the art cannot recognize the metes and bounds set forth by the term "high catalytic activity" because "high" is a relative term, thus rendering claim 18 indefinite.

The symbol "H" in claim 17, line 4 is not defined either within the claim or in the specification. Thus, it remains unknown to the examiner what is meant by "H", rendering the claim and its dependent claims indefinite.

Claim 21, lines 2-3 recite "wherein the reaction is carried out by using further DNA as the antisense molecule". It is unclear what is meant by "further DNA" since the instant disclosure is silent about the specific structures of the recited "further DNA". Thus, one of ordinary skill in the art cannot determine the metes and bounds set forth by the claim language.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of aminoacylating a tRNA *in vitro*, does not reasonably provide enablement for a method of aminoacylating a tRNA *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not

be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on both *in vivo* and *in vitro* methods as contemplated by the statement "it is a matter of course that hits method can also be applied to natural amino acids". See page 1 of specification. Nevertheless, the instant disclosure provides aminoacylating methods performed *in vitro* but not *in vivo.* Since it is an art-recognized fact that the bioavailability as well as the activity of nucleic acid compositions are highly unpredictable in real physiological conditions *in vivo,* the amount of direction/guidance (i.e., working examples) provided by the inventor must be sufficient to overcome the art-recognized unpredictability of nucleic acids *in vivo.* See, for example, Opalinska et al. (*Nature Reviews Drug Discovery*, 2002, 1:503-514).

> "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA" (page 511)

Given such unpredictability of whether the nucleic acids administered *in vivo* would properly access and hybridize with the target genomic DNA as taught by Opalinska et al., one of

ordinary skill in the art would require specific guidance by the inventors so as to practice the instantly claimed invention without undue experimentation. The instant disclosure is silent about any *in vivo* application of the claimed invention, thus it does not provide sufficient amount of direction to overcome the art-recognized unpredictability of using nucleic acids *in vivo*. Accordingly, in view of the totality of the factors listed on page 7 herein, it is concluded that the one of skill in the art cannot practice the invention commensurate in scope with the instant claims without undue experimentation and therefore, claims 12-15 and 17-21 are enabled only as far as *in vitro* methods of aminoacylation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 102(a) as being anticipated by Ninomiya et al. (*Nucleic Acids Research Supplement,* 2002, applicant's citation No. CB submitted in FORM PTO/SB/08a/b, filed on March 9, 2005).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

The claims are drawn to an aminoacylation method wherein a tRNA is aminoacylated through a ternary system of binding reaction involving tRNA, aminoacyl-PNA, and DNA.

Ninomiya et al. teach aminoacylation method through formation of tRNA/DNA/aa-PNA. See that Figure 1 is so close in its content to Figure 2(b) of the instant application, both of which illustrate the instantly claimed invention. They also teach the compound of Figure 2, which reads on the instantly claimed formula [1] in claim 17. Ninomiya teach all the active steps of the instantly claimed invention including a step wherein the aminoacylation reaction is terminated (page 102, right column) and a step wherein the aminoacylation reaction involving transesterification is performed at around a neutral pH (pH6.5). See page 102, left column.

Accordingly, the teachings of Ninomiya et al. anticipate the instantly claimed methods.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 102(a) as being anticipated by Suzuki et al. (*The Chemical Society of Japan Koen Yokoshu*, 2003, applicant's citation No. CG submitted in FORM PTO/SB/08a/b, filed on March 9, 2005).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

The claims are describe above.

The boxed figure in the middle of the reference of Suzuki et al. represents the instantly claimed invention, which involves a ternary hybridization of tRNA-DNA-aminoacyl-PNA. Further, the compound represented in Figure 1 of Suzuki et al. reads on the compound of formula [1] claimed in claim 17. Since Suzuki et al. perform the active steps of the instant invention and

teach the ingredients of the claimed aminoacylation method, it is concluded that the instantly claimed invention is anticipated by Suzuki et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

Dana TC1600

JANE ZARA, PH.D.
PRIMARY EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 37 CFR §1.821(g). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. §§1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. §§1.821-1.825. Applicants attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a Sequence Listing as required by 37 C.F.R. §1.821(c).
- [X] 3. A copy of the Sequence Listing in computer readable form has not been submitted as required by 37 C.F.R. §1.821(e).
- [ ] 4. A copy of the Sequence Listing in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. §1.822 and/or 1.823, as indicated on the attached copy of the marked-up Raw Sequence Listing.
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. §1.825(d).
- [ ] 6. The paper copy of the Sequence Listing is not the same as the computer readable from of the Sequence Listing as required by 37 C.F.R. §1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the Sequence Listing. (If the unidentified sequences are not provided on the CRF)
- [X] An initial or substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification. (If the unidentified sequences are not provided in the paper copy)
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). (If a new paper and/or CRF are required)

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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